

CLAIMS

We claim:

1. A method for identifying receptors, comprising:

- 5 (a) introducing a first polynucleotide encoding a receptor in to a cell, wherein the receptor comprises a ligand binding domain for a target ligand operably linked to a polynucleotide binding domain so that binding of the target ligand to the receptor activates transcription of a second polynucleotide complementing a selection agent; and
- 10 (b) culturing the cell on the selective media in the presence of the target ligand, wherein growth of the cell indicates interaction of the receptor with the target ligand.

2. The method of claim 1, further comprising culturing the cell on

- 15 selective media in the absence of the target ligand, wherein growth of the cell indicates the receptor constitutively activates transcription of the second polynucleotide.

20 3. A cell comprising:

- (a) a recombinant nuclear receptor that induces expression of a first polynucleotide in response to interaction with a target small molecule, wherein expression of the first polynucleotide complements a selective agent; and
- 25 (b) an adapter fusion protein comprising a human coregulator domain operably linked to an activation domain, wherein the adapter fusion protein enhances transcription of the first polynucleotide induced by the recombinant nuclear receptor.

30 4. The cell of claim 3, wherein the cell is a yeast cell.

5. The cell of claim 3, wherein the human coregulator domain is a coactivator domain selected from the group consisting of SRC-1 and ACTR.

6. A method for identifying enzymes comprising:

(a) introducing a first polynucleotide into a cell that is unable to grow on selective media, wherein the cell expresses a recombinant receptor polypeptide that activates transcription of a second polynucleotide in response to interaction of the recombinant receptor polypeptide with a target substance and wherein the first polynucleotide encodes a polypeptide that produces the target substance;

(b) culturing the cell on the selective media; and

(c) selecting the cell that grows on the selective media.

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7. The method of claim 6, wherein the selective media does not contain an amino acid necessary for survival.

8. The method of claim 7, wherein the amino acid is selected from the group consisting of histidine and alanine.

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9. The method of claim 6, wherein the first polynucleotide encodes an enzyme that produces the target substance.

10. The method of claim 6, wherein the first polynucleotide encodes an engineered enzyme.

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11. The method of claim 6, wherein the first polynucleotide encodes a naturally occurring enzyme.

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12. The method of claim 6, wherein the transformed cell further expresses an adaptor fusion protein comprising a human coregulator domain operably linked to an activation domain, wherein the adaptor fusion protein enhances transcription of the first polynucleotide induced by the recombinant receptor polypeptide.

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13. The method of claim 6, wherein the adaptor fusion protein comprises a human coactivator for transcription of the second polynucleotide.

14. The method of claim 6, wherein introducing a first polynucleotide into the cell comprises introducing a plurality of polynucleotides encoding enzymes having different substrates into the cell, and wherein growth of a cell on the selective media indicates that the plurality of polynucleotides encode enzymes for producing products that complement the selective media.

15. The method of claim 14, wherein the product of one of the enzymes is the substrate of another of the enzymes.

16. A method for selecting cells comprising:

(a) introducing a first polynucleotide into a cell, wherein the cell expresses a recombinant receptor polypeptide that activates transcription of a second polynucleotide in response to interaction of the recombinant receptor polypeptide with a target substance;

(b) culturing the cell on selective media in the presence of a first selection agent; and

(c) selecting the cell that survives on the selective media in the presence of the selection agent, wherein expression of the second polynucleotide inhibits growth of the cell.

17. The method of claim 16, wherein the second polynucleotide encodes a cytotoxic polypeptide.

18. The method of claim 17, wherein the cytotoxic polypeptide comprises a proapoptotic polypeptide.

19. The method of claim 16, wherein the first selective agent comprises 5-fluoroorotic acid.

20. The method of claim 19, wherein the second polynucleotide encodes orotidine-5'-phosphate decarboxylase and wherein a toxic substance produced by the orotidine-5'-phosphate decarboxylase comprises 5-fluorouracil.